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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,193	09/29/2005	Genevieve Andre-Fontaine	033339/292053	9098

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EXAMINER	
RUSSEL, JEFFREY E	
ART UNIT	**PAPER NUMBER**
1654	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,193	ANDRE-FONTAINE ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6-16,20-23 and 26-29* is/are pending in the application.

4a) Of the above claim(s) *7-16,20,23 and 26-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6,21,22 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Applicant's election with traverse of the invention of Group I, claims 1-6, and claims 21-22 (in part) in the reply filed on November 13, 2007 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-16, 20, 23, and 26-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 13, 2007.

This application contains claims 7-16, 20, 23, and 26-28 drawn to an invention nonelected with traverse in the reply filed on November 13, 2007. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1, 4, 6, 21, 22, and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the peptide represented by SEQ ID NO:1, the pharmaceutically acceptable salts of this peptide, and the peptide coupled to a carrier protein, does not reasonably provide enablement for homologs of this peptide, peptides comprising less than the 25 amino acid of SEQ ID NO:1, and functional fragments of the peptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150 (CCPA 1977)

and have been adopted by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. With respect to (1), the nature of the invention is a peptide vaccine for Leptospirosis. With respect to (2), Applicants disclose at page 5, lines 28-30, of the specification that the state of the prior art is that whole bacteria are necessary to provide antigens. This contrasts with the instant claims, in which individual compounds are used to provide antigens. With respect to (3), the relative skill of those in the art is high. With respect to (4), the predictability of the vaccine art is relatively low. Applicants state at page 2, lines 7-10, that it is particularly difficult to combat Leptospirosis infections due to their bacteriological complexity and due to the diversity of animals which can be infected by the bacteria. With respect to (5), the breadth of the claims is relatively large. The claims embrace compounds in which up to 20% of the amino acids of the peptide of SEQ ID NO:1 are altered (i.e. in order to form homologs); and in which up to five amino acids are deleted from the peptide of SEQ ID NO:1 (i.e. in order to form homologs or functional fragments). With respect to (6) and (7), Applicants' specification discloses working examples demonstrating the utility and enablement of the peptide of SEQ ID NO:1. However, Applicants' specification does not provide working examples, in vivo or in vitro or otherwise, for any other compound. Applicants' specification does not provide any structure-function relationship so that one of skilled in the art would reasonably know which portions of the peptide of SEQ ID NO:1 would have to be preserved in

order to retain activity. With respect to (8), the quantity of experimentation necessary to use the entire claimed invention would be vast. Jones (U.S. Patent Application Publication 2003/0186887) shows that epitopes generally range in size from 3 to 10 amino acids. See paragraph [0008]. Accordingly, the changes in the peptide of SEQ ID NO:1 recited in Applicants' claims could easily alter or eliminate epitopes which are necessary for activity. In the absence of any disclosed structure-function relationship, one skilled in the art would be limited essentially to random testing of all possible changes to the peptide of SEQ ID NO:1 in order to determine whether a particular compound can be used as a vaccine for Leptospirosis. Such random testing constitutes undue experimentation. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

4. Claims 1, 4, 6, 21, 22, and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear if claim 1, lines 2-4, should be interpreted as open or closed language. It is not clear if "a peptide" embraces larger peptides which comprise one or more amino acids in addition to those represented by SEQ ID NO:1. Note that dependent claim 6 recites that a carrier protein can be to be coupled to the compound of claim 1, i.e. to the peptide or homolog. If a carrier protein, often comprising hundreds of amino acids, can be added to the peptide of SEQ ID NO:1 or to the homolog in the dependent claims, it would appear that an unlimited number of amino acids could be added to the peptide of SEQ ID NO:1 or to the homolog in the independent claim.

5. Claims 1, 4, 6, 21, 22, and 29 are objected to because of the following informalities: Claim 1 ends with a comma rather than with a period. Appropriate correction is required.

6. Claims 4, 6, and 29 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Assuming that claim 1, lines 2-4, should be interpreted as closed language, i.e. that the peptide consists of the 25 amino acids of SEQ ID NO:1 and that the homologs consist of 20 to 30 amino acids, then dependent claims 4, 6, and 29 are improper dependent claims, because there is no language or limitation in the independent claims which permits the deletion of any number of amino acids from the peptide of SEQ ID NO:1, which embraces coupling of a carrier protein to the peptide of SEQ ID NO:1 (or to its homologs), or which embraces forming salts of the peptide of SEQ ID NO:1 or its homologs. Note that the pharmaceutically acceptable salt and functional fragment limitations have been deleted from the independent claim.

7. Claims 1, 4, 6, 21, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 01/59123. (The examiner relies upon U.S. Patent Application Publication 2003/0124567 as a translation of the WO Patent Application '123. All citations in this rejection will be to the text of the translation.) The WO Patent Application '123 teaches a PPL protein of 32 kDa and comprising SEQ ID NO:7, whose residues at positions 153-177 are 100% similar to Applicants' SEQ ID NO:1. The WO Patent Application '123 also teaches immunogenic compositions comprising the protein, and the protein immobilized on solid supports. See, e.g., paragraphs [0024], [0067], [0070], [0086], and [0089], and claims 3 and 29

of the translation. Assuming that Applicants' claims do not exclude compounds in which additional amino acids are added to either terminus of the peptide represented by SEQ ID NO:1 (see also the above rejection under 35 U.S.C. 112, second paragraph), the PPL protein of the WO Patent Application '123 anticipates Applicants' claimed compounds/peptides. With respect to instant claim 6, the fragments at residues 1-152 and 178-280 of the PPL protein of the WO Patent Application '123 correspond to Applicants' carrier protein.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

9. Claim 29 is rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 01/59123 as applied against claims 1, 4, 6, 21, and 22 above, and further in view of Dyrsting et al (U.S. Patent No. 6,077,822). The WO Patent Application '123 does not teach its PPL protein in salt form. Dyrsting et al teach that it is common in the pharmaceutical industry to use salt forms of drugs, e.g., because of their higher solubility or greater bioavailability. See column 1, lines 18-27. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form a salt from the PPL protein of the WO Patent Application '123 because Dyrsting et al teach that this is a common practice with the benefit of higher solubility or greater bioavailability.

10. Applicant's arguments filed May 14, 23008 have been fully considered but they are not persuasive.

The rejection under 35 U.S.C. 112, first paragraph, is maintained, essentially for the reasons of record. As noted in the rejection and repeated by Applicants at page 9 of the response, the predictability of antigen/vaccine creation is very low. Applicants state that "it was not therefore expected that a small fragment of the complete PPL would induce immunity to the pathogenic bacteria responsible for Leptospirosis". Given the lack of predictability and the unexpectedness of Applicants' result for a peptide represented by SEQ ID NO:1, it remains unpredictable as to whether even smaller fragments of this peptide, or whether variations of this peptide with up to five altered amino acids, would also be capable of inducing immunity to the pathogenic bacteria responsible for Leptospirosis. Applicants point to Example 3-1 as demonstrating that a variant of SEQ ID NO:1 is capable of inducing the desired immune response. However, this example demonstrates the effectiveness of the intact peptide coupled to

a carrier protein, which the rejection already indicates is enabled subject matter. The example does not demonstrate the effectiveness of peptide fragments or of the peptide with an altered amino acid sequence.

The rejection under 35 U.S.C. 112, second paragraph, is maintained. Applicants contend that Claim 1 has been amended to closed language. However, Applicants do not point to any actual language in claim 1 which is indicative of closed language. The only change to the language of claim 1, other than the deletion of some alternative products, is the change from the definite article "the" to the indefinite article "a". An indefinite article is not indicative of closed language. Mere cancellation of dependent claims does not alter the scope of the independent claim upon which they depend. The issue of whether or not closed language is present in the independent claim is important in the determination of whether or not claims 4, 6, and 29 properly depend upon the independent claim. The issue is also important in the determination of whether or not the WO Patent Application 01/59123 continues to anticipate the claims.

The objection under 37 CFR 1.75(c) is maintained. Claim 6 is silent as to whether the peptide coupled to the carrier protein comprises a single amino acid residue backbone - the claim embraces both possibilities. In any event, assuming that the independent claim is to be interpreted as using closed language, then the independent claim does not permit any further modification of the peptide or homologs which would result in the formation of a different compound. Modification of the peptide or homologs with a carrier protein, regardless of whether a single amino acid residue backbone is formed or not, results in the formation of a different compound not encompassed within the scope of the independent claim.

The rejection under 35 U.S.C. 102(b) based upon the WO Patent Application 01/59123 is maintained. Assuming that it is ultimately determined that claim 1 uses closed language in defining its compound, then the examiner agrees that the WO Patent Application '123 will no longer anticipate or render obvious instant claims 1, 4, 21, 22, or 29. However, the rejection of claim 6 over the WO Patent Application '123 would be maintained. Applicants have provided no explanation as to why the claimed peptide coupled to a carrier protein does not embrace the intact PPL protein of the reference.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications

such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey E. Russel/
Primary Examiner, Art Unit 1654

JRussel
July 8, 2008